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Jennifer L. Purnell

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Lieven Stuyver
Joost Louwagie
Rudi Rossau

Serial No.:

Filed: Herewith

For: METHOD FOR THE DETECTION OF DRUG-INDUCED MUTATIONS IN THE REVERSE TRANSCRIPTASE GENE

Group Art Unit:

Examiner:

Atty. Dkt. No.: INNS:008—3
11362.0008.DVUS02

PRELIMINARY AMENDMENT

BOX PATENT APPLICATION
Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination, please amend this application as follows:

IN THE SPECIFICATION:

At page 1, line 3 after the title, please insert the following new paragraph:

--This is a divisional of co-pending application Serial No. 09/580,794 filed May 30, 2000, which is a divisional of Serial No. 08/913,833, filed September 15, 1997, now issued as Patent No. 6,078,093, which is a §371 national application of PCT/EP97/00211 filed January 17, 1997, which claims priority under 35 USC §119 to EP 96 870081.5 filed June 25, 1996 and EP 96 870005.4 filed January 26, 1996.—

At page 1, following the above inserted paragraph, please add the heading:

--BACKGROUND OF THE INVENTION--.

At page 2, line 16, please insert the heading:

--BRIEF SUMMARY OF THE INVENTION--.

At page 5, line 7, please insert the following headings and nine paragraphs:

--BRIEF DESCRIPTION OF THE FIGURES

Figure 1: Natural and drug induced variability in the vicinity of codons 41, 50, 67-70, 74-75, 150, 181-184, 215 and 219 of the HIV RT gene. The most frequently observed wild-type sequence is shown in the top line. Naturally occurring variations are indicated below. Drug-induced variants are indicated in bold italics.

Figure 2 A. Reactivities of the selected probes for codon 41 immobilized on LiPA strips with reference material. The position of each probe on the membrane strip is shown at the right of each panel. The sequence of the relevant part of the selected probes is given in Table 4. Each strip is incubated with a biotinylated PCR fragment from the reference panel. The reference panel accession numbers are indicated in Table 4. For several probes multiple reference panel possibilities are available, but only one relevant accession number given each time. *: False

positive reactivities. On top of the strips, the amino acids at the relevant codon, as derived from the probe reactivity, is indicated.

Figure 2 B. Reactivities of the selected probes for codons 69-70 immobilized on LiPA strips with reference material. The position of each probe on the membrane strip is shown at the right of each panel. The sequence of the relevant part of the selected probes is given in Table 4. Each strip is incubated with a biotinylated PCR fragment from the reference panel. The reference panel accession numbers are indicated in Table 4. For several probes multiple reference panel possibilities are available, but only one relevant accession number given each time. *: False positive reactivities. On top of the strips, the amino acids at the relevant codon, as derived from the probe reactivity, is indicated.

Figure 2 C. Reactivities of the selected probes for codons 74-75 immobilized on LiPA strips with reference material. The position of each probe on the membrane strip is shown at the right of each panel. The sequence of the relevant part of the selected probes is given in Table 4. Each strip is incubated with a biotinylated PCR fragment from the reference panel. The reference panel accession numbers are indicated in Table 4. For several probes multiple reference panel possibilities are available, but only one relevant accession number given each time. On top of the strips, the amino acids at the relevant codon, as derived from the probe reactivity, is indicated.

Figure 2 D. Reactivities of the selected probes for codons 184 immobilized on LiPA strips with reference material. The position of each probe on the membrane strip is shown at the right of each panel. The sequence of the relevant part of the selected probes is given in Table 4. Each strip is incubated with a biotinylated PCR fragment from the reference panel. The reference panel accession numbers are indicated in Table 4. For several probes multiple reference panel possibilities are available, but only one relevant accession number given each time. On top of the strips, the amino acids at the relevant codon, as derived from the probe reactivity, is indicated.

Figure 2 E. Reactivities of the selected probes for codons 215 immobilized on LiPA strips with reference material. The position of each probe on the membrane strip is shown at the right of each panel. The sequence of the relevant part of the selected probes is given in Table 4. Each

strip is incubated with a biotinylated PCR fragment from the reference panel. The reference panel accession numbers are indicated in Table 4. For several probes multiple reference panel possibilities are available, but only one relevant accession number given each time. On top of the strips, the amino acids at the relevant codon, as derived from the probe reactivity, is indicated.

Figure 2 F. Reactivities of the selected probes for codons 219 immobilized on LiPA strips with reference material. The position of each probe on the membrane strip is shown at the right of each panel. The sequence of the relevant part of the selected probes is given in Table 4. Each strip is incubated with a biotinylated PCR fragment from the reference panel. The reference panel accession numbers are indicated in Table 4. For several probes multiple reference panel possibilities are available, but only one relevant accession number given each time. On top of the strips, the amino acids at the relevant codon, as derived from the probe reactivity, is indicated.

Figure 3. Clinical and virological features detectable in three patient follow-up samples. All three patients were infected with a HIV-1 strain showing the M41-T69-K70-L74-V75-M184-F214-T215-K219 genotype (wild type pattern). Top: Fluctuations between plasma HIV RNA copy numbers (■) and CD4 cell count (x) are given in function of time. The different treatment regimens and the period of treatment is indicated on top. Middle: Changes that appeared during the treatment period and that could be scored by means of the LiPA probes are indicated, for patient 91007 at codon 41 and 215; for patient 94013 at codon 184; for patient 92021 at codon 70, 214, 215, 219. Bottem: Corresponding LiPA strips for a subset of the aa changes are shown. LiPA probes are indicated on the left, the aa interpretation is indicated at the right of each panel.

Figure 4. Reactivities of the selected probes for codons 151 and 181 on LiPA strips with reference material. The position of each probe on the membrane strip is shown at the right of each panel. The sequence of the relevant part of the selected probes is given in Table 3. LiPA strips were incubated with sequence-confirmed PCR fragments, extracted and amplified from: a wild-type HIV-1 isolate (strip 1), a wild-type isolate with a polymorphism at codon 151 (strip 2) or 149 (strip 3), a multi-drug resistant HIV-1 isolate (strip 4) with no information about codon

181 and a non-nucleoside analogue treated HIV-1 isolate which remained wild-type at codon 151 (strip5).

DETAILED DESCRIPTION OF THE INVENTION—

At page 18, line 29, through page 21, line 12, please delete the heading "FIGURE AND TABLE LEGENDS" and the text describing the drawings.

At page 23, please delete the paragraph at lines 9-27 and replace with the following:

--For cDNA synthesis and PCR amplification, the RNA pellet was dissolved in 15 μl random primers (20 ng/μl, pdN_6, Pharmacia), prepared in DEPC-treated or HPLC grade water. After denaturation at 70°C for 10 minutes, 5 μl cDNA mix was added, composed of 4 μl 5x AMV-RT buffer (250mM Tris.HC1 pH 8.5, 100mM KC1, 30mM $MgCl_2$, 25 mM DTT), 0.4 μL 25mM dXTPs, 0.2 μl or 25U Ribonuclease Inhibitor (HPRI, Amersham), and 0.3 μl or 8U AMV-RT (Stratagene). CDNA synthesis occurred during the 90 minutes incubation at 42°C. The HIV RT gene was then amplified using the following reaction mixture. 5 μl cDNA, 4.5 μl 10x Taq buffer, 0.3 μl 25 mM dXTPs, 1 μl (10 pmol) of each PCR primer, 38 μl H_2O, and 0.2 μl (1 U) Taq. The primers for amplification had the following sequence: outer sense RT-9: 5' bio-GTACAGTATTAGTAGGACCTACACCTGTC 3' (SEQ ID NO 162); nested sense RT-1: 5' bio-CCAAAAGTTAAACAATGGCCATTGACAGA 3' (SEQ ID NO 163); nested antisense RT-4: 5' bio-AGTTCATAACCCATCCAAAG 3' (SEQ ID NO 164); and outer antisense primer RT-12: 5' bio-ATCAGGATGGAGTTCATAACCCATCCA 3' (SEQ ID NO 39). Annealing occurred at 57°C, extension at 72°C and denaturation at 94°C. Each step of the cycle took 1 minute, the outer PCR contained 40 cycles, the nested round 35. Nested round PCR products were analysed on agarose gel and only clearly visible amplification products were used in the LiPA procedure. Quantification of viral RNA was obtained with the HIV Monitor™test (Roche, Brussels, Belgium).--

IN THE CLAIMS:

Please cancel claims 1-14 without prejudice.

Please amend claims 15 and 16 to read as follows:

15. (Amended) A kit for inferring the nucleotide sequence at codons of interest in the HIV RT gene and/or the amino acids corresponding to these codons and/or the antiviral drug resistance spectrum of HIV isolates present in a biological sample comprising the following components:

(i) optionally, a means for releasing, isolating or concentrating the polynucleic acids present in said sample;

(ii) optionally, at least one suitable set of primers;

(iii) at least two different probes, wherein each probe is capable of hybridizing specifically to one or more target codons within any region I to VIII as represented in Figure 1, said probes optionally fixed to a solid support;

(iv) a hybridization buffer, or components necessary for producing said buffer;

(v) a wash solution, or components necessary for producing said solution;

(vi) optionally, a means for detecting the hybrids resulting from the preceding hybridization;

(vii) optionally, a means for attaching said probe to a solid support.

16. (Amended) A kit for inferring the HIV RT resistance spectrum of HIV in a biological sample, coupled to the identification of the HIV isolate involved, comprising the following components:

(i) optionally, a means for releasing, isolating or concentrating the polynucleic acids present in said sample;

(ii) optionally, at least one suitable set of primers;

(iii) at least two different probes, wherein each probe is capable of hybridizing specifically to one or more target codons within any region I to VIII as represented in Figure 1, said probes optionally fixed to a solid support;

(iv) a hybridization buffer, or components necessary for producing said buffer;

(v) a wash solution, or components necessary for producing said solution;

(vi) optionally, a means for detecting the hybrids resulting from the preceding hybridization;

(vii) optionally, a means for attaching said probe to a solid support.

Please add new claims 17-42 as follows:

--17. (New) The kit according to claims 15 or 16, wherein the primer is selected from the group consisting of SEQ ID No: 162, 163, 164 and 39.

18. (New) The kit according to claims 15 or 16, wherein the set of primers is selected from the group consisting of

SEQ ID No: 162 and 163, and

SEQ ID No: 164 and 39.

19. (New) A kit for inferring the nucleotide sequence at codons of interest in the HIV RT gene and/or the amino acids corresponding to these codons and/or the antiviral drug resistance spectrum of HIV isolates present in a biological sample, the kit comprising the following components:

at least two different probes, wherein the probes are selected from the group consisting of

SEQ ID NO: 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 30, 31, 32, 33, 34, 35, 37, 40, 41, 44, 45, 46, 47, 48, 49, 50, 51, 52, 54, 55, 56, 57, 58, 59, 61, 62, 63, 64, 65, 66, 67, 68, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 114, 115, 117, 118, 119, 120, 121, 122, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 138, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 154, 155, 156, 157 and 159;

a hybridization buffer, or components necessary for producing said buffer; and

a wash solution, or components necessary for producing said solution.

20. (New) A kit for inferring the HIV RT resistance spectrum of HIV in a biological sample, coupled to the identification of the HIV isolate involved, comprising the following components:

at least two different probes, wherein the probes are selected from the group consisting of SEQ ID NO: 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 30, 31, 32, 33, 34, 35, 37, 40, 41, 44, 45, 46, 47, 48, 49, 50, 51, 52, 54, 55, 56, 57, 58, 59, 61, 62, 63, 64, 65, 66, 67, 68, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 114, 115, 117, 118, 119, 120, 121, 122, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 138, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 154, 155, 156, 157 and 159;

a hybridization buffer, or components necessary for producing said buffer; and

a wash solution, or components necessary for producing said solution.

21. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein the probes are selected from the group consisting of SEQ ID NO: 4, 8, 9, 10, 11, 12, 13, 14, 15, 19, 21, 22, 24, 25, 27, 28, 30, 31, 32, 33, 34, 35, 40, 46, 48, 49, 50, 51, 52, 54, 55, 56, 57, 58, 70, 72, 73, 75, 76, 78, 79, 80, 81, 82, 83, 86, 88, 90, 93, 95, 96, 97, 98, 99, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 115, 117, 118, 119, 120, 121, 122, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 138, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 154, 155, 157 and 159.

22. (New) The kit according to any one claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 4, 8, 9, 10, 11, 12, 13, 14, 15, 19, 21, 22, 24, 25, 27 and 28.

23. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 30, 31, 32, and 33.

24. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 34, 35, 40, 46, 48, 49, 50, 51 and 52.

25. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 57 and 58.

26. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 70, 72, 73, 75, 76, 78, 79, 80, 81, 82 and 83.

27. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 86, 88, 90, 93, 95, 96, 97, 98, 99, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 115, 117, 118, 119, 120, 121, 122, 124, 125, 126, 127, 128, 130, 131, 132, 133, 134, 135 and 136.

28. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 138, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 154, 155, 157 and 159.

29. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 5, 6, 7, 16, 17, 18, 20, 23, 26, 37, 41, 44, 45, 47, 54, 55, 56, 59, 61, 62, 63, 64, 65, 66, 67, 68, 71, 74, 77, 84, 85, 87, 89, 91, 92, 94, 100, 114, 128, 129, 138 and 156.

30. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 5, 6, 7, 16, 17, 18, 20, 23 and 26.

31. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 37, 41, 44, 45 and 47.

32. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 54, 55, 56 and 59.

33. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 61, 62, 63 and 64.

34. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 65, 66, 67, 68, 71, 74, 77 and 84.

35. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 85, 87, 89, 91, 92, 94, 100, 114, 128 and 129.

36. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 138 and 156.

37. (New) The kit of claims 19 or 20, further comprising a means for releasing, isolating, or concentrating polynucleic acids present in the sample.

38. (New) The kit of claims 19 or 20, further comprising at least one suitable set of primers.

39. (New) The kit according to claim 38, wherein the primer is selected from the group consisting of SEQ ID No: 162, 163, 164 and 39.

40. (New) The kit according to claim 38, wherein the set of primers is selected from the group consisting of

SEQ ID No: 162 and 163, and

SEQ ID No: 164 and 39.

41. (New) The kit of claims 19 or 20, wherein at least two probes are fixed to a solid support.

42. (New) The kit of claims 19 or 20, further comprising a means for detecting hybrids resulting from hybridization of at least one of the two probes to the sample.--

REMARKS

I. Status of the Claims and Rationale for the Amendment

The parent application, U.S. Patent Application Serial No. 09/580,794, was allowed on April 23, 2001 but has not yet issued.

The specification has been amended to recite the relationship with the parent cases and to incorporate formalities required by the examiner in the parent case. Support for the paragraphs inserted at page 5, line 7, is found at page 18, line 30 through page 21, line 2 of the original Specification. The paragraph at page 23, lines 9-27 has been amended to reflect the correct SEQ ID Nos. A marked up version of the replacement paragraph at page 23, lines 9-27 is shown in the attached **Marked Up Version of the Specification**. Support for the Abstract added to page 47 is found on the cover page of the original application PCT/EP97/00211.

The active claims in this case are claims 15-42. Claims 15 and 16 are amended. The new claims 17-42 are directed to kits containing primers and probes corresponding to the allowed claims of Serial No. 09/580,794 and Patent No. 6,087,093. **A Marked Up Set of Claim Amendments** is attached.

II. Sequence Listing

Also transmitted herewith is a diskette containing the computer readable form of those sequences in the specification, a verified statement in accordance with the sequence rules, and a separate paper copy of the sequence listing.

It is believed that no fee is due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Commissioner is authorized to deduct said fees from Deposit Account No. 01-2508/11362.0008.DVUS02.

Respectfully submitted,

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Date: August 31, 2001

MARKED UP SET OF REPLACEMENT PARAGRAPHS

Page 23, lines 9-27:

For cDNA synthesis and PCR amplification, the RNA pellet was dissolved in 15 μl random primers (20 ng/μl, pdN_6, Pharmacia), prepared in DEPC-treated or HPLC grade water. After denaturation at 70°C for 10 minutes, 5 μl cDNA mix was added, composed of 4 μl 5x AMV-RT buffer (250mM Tris.HC1 pH 8.5, 100mM KC1, 30mM $MgCl_2$, 25 mM DTT), 0.4 μL 25mM dXTPs, 0.2 μl or 25U Ribonuclease Inhibitor (HPRI, Amersham), and 0.3 μl or 8U AMV-RT (Stratagene). CDNA synthesis occurred during the 90 minutes incubation at 42°C. The HIV RT gene was then amplified using the following reaction mixture. 5 μl cDNA, 4.5 μl 10x Taq buffer, 0.3 μl 25 mM dXTPs, 1 μl (10 pmol) of each PCR primer, 38 μl H_2O, and 0.2 μl (1 U) Taq. The primers for amplification had the following sequence: outer sense RT-9: 5' bio-GTACAGTATTAGTAGGACCTACACCTGTC 3' (SEQ ID NO ~~96~~ **162**); nested sense RT-1: 5' bio-CCAAAAGTTAAACAATGGCCATTGACAGA 3' (SEQ ID NO ~~97~~ **163**); nested antisense RT-4: 5' bio-AGTTCATAACCCATCCAAAG 3' (SEQ ID NO ~~98~~ **164**); and outer antisense primer RT-12: 5' bio-ATCAGGATGGAGTTCATAACCCATCCA 3' (SEQ ID NO ~~99~~ **39**). Annealing occurred at 57°C, extension at 72°C and denaturation at 94°C. Each step of the cycle took 1 minute, the outer PCR contained 40 cycles, the nested round 35. Nested round PCR products were analysed on agarose gel and only clearly visible amplification products were used in the LiPA procedure. Quantification of viral RNA was obtained with the HIV Monitor™test (Roche, Brussels, Belgium).

MARKED UP SET OF CLAIM AMENDMENTS

15. (Amended) A kit for inferring the nucleotide sequence at codons of interest in the HIV RT gene and/or the amino acids corresponding to these codons and/or the antiviral drug resistance spectrum of HIV isolates present in a biological sample comprising the following components:

(i) [when appropriate] optionally, a means for releasing, isolating or concentrating the polynucleic acids present in said sample;

(ii) [when appropriate] optionally, at least one [of the above-defined] suitable set of primers;

(iii) [at least two of the probes as defined above, possibly fixed to a solid support] at least two different probes, wherein each probe is capable of hybridizing specifically to one or more target codons within any region I to VIII as represented in Figure 1, said probes optionally fixed to a solid support;

(iv) a hybridization buffer, or components necessary for producing said buffer;

(v) a wash solution, or components necessary for producing said solution;

(vi) [when appropriate] optionally, a means for detecting the hybrids resulting from the preceding hybridization;

(vii) [when appropriate] optionally, a means for attaching said probe to a solid support.

16. (Amended) A kit for inferring the HIV RT resistance spectrum of HIV in a biological sample, coupled to the identification of the HIV isolate involved, comprising the following components:

(i) [when appropriate] optionally, a means for releasing, isolating or concentrating the polynucleic acids present in said sample;

(ii) [when appropriate] optionally, at least one [of the above-defined] suitable set of primers;

(iii) [at least two of the probes as defined above, possibly fixed to a solid support] at least two different probes, wherein each probe is capable of hybridizing

specifically to one or more target codons within any region I to VIII as represented in Figure 1, said probes optionally fixed to a solid support;

(iv) a hybridization buffer, or components necessary for producing said buffer;

(v) a wash solution, or components necessary for producing said solution;

(vi) [when appropriate] optionally, a means for detecting the hybrids resulting from the preceding hybridization;

(vii) [when appropriate] optionally, a means for attaching said probe to a solid support.

17. (New) The kit according to claims 15 or 16, wherein the primer is selected from the group consisting of SEQ ID No: 162, 163, 164 and 39.

18. (New) The kit according to claims 15 or 16, wherein the set of primers is selected from the group consisting of

SEQ ID No: 162 and 163, and

SEQ ID No: 164 and 39.

19. (New) A kit for inferring the nucleotide sequence at codons of interest in the HIV RT gene and/or the amino acids corresponding to these codons and/or the antiviral drug resistance spectrum of HIV isolates present in a biological sample, the kit comprising the following components:

at least two different probes, wherein the probes are selected from the group consisting of

SEQ ID NO: 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 30, 31, 32, 33, 34, 35, 37, 40, 41, 44, 45, 46, 47, 48, 49, 50, 51, 52, 54, 55, 56, 57, 58, 59, 61, 62, 63, 64, 65, 66, 67, 68, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 114, 115, 117, 118, 119, 120, 121, 122, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 138, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 154, 155, 156, 157 and 159;

a hybridization buffer, or components necessary for producing said buffer; and

a wash solution, or components necessary for producing said solution.

21. (New) A kit for inferring the HIV RT resistance spectrum of HIV in a biological sample, coupled to the identification of the HIV isolate involved, comprising the following components:

at least two different probes, wherein the probes are selected from the group consisting of SEQ ID NO: 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 30, 31, 32, 33, 34, 35, 37, 40, 41, 44, 45, 46, 47, 48, 49, 50, 51, 52, 54, 55, 56, 57, 58, 59, 61, 62, 63, 64, 65, 66, 67, 68, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 114, 115, 117, 118, 119, 120, 121, 122, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 138, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 154, 155, 156, 157 and 159;

a hybridization buffer, or components necessary for producing said buffer; and

a wash solution, or components necessary for producing said solution.

21. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein the probes are selected from the group consisting of SEQ ID NO: 4, 8, 9, 10, 11, 12, 13, 14, 15, 19, 21, 22, 24, 25, 27, 28, 30, 31, 32, 33, 34, 35, 40, 46, 48, 49, 50, 51, 52, 54, 55, 56, 57, 58, 70, 72, 73, 75, 76, 78, 79, 80, 81, 82, 83, 86, 88, 90, 93, 95, 96, 97, 98, 99, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 115, 117, 118, 119, 120, 121, 122, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 138, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 154, 155, 157 and 159.

22. (New) The kit according to any one claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 4, 8, 9, 10, 11, 12, 13, 14, 15, 19, 21, 22, 24, 25, 27 and 28.

23. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 30, 31, 32, and 33.

24. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 34, 35, 40, 46, 48, 49, 50, 51 and 52.

25. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 57 and 58.

26. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 70, 72, 73, 75, 76, 78, 79, 80, 81, 82 and 83.

27. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 86, 88, 90, 93, 95, 96, 97, 98, 99, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 115, 117, 118, 119, 120, 121, 122, 124, 125, 126, 127, 128, 130, 131, 132, 133, 134, 135 and 136.

28. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 138, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 154, 155, 157 and 159.

29. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 5, 6, 7, 16, 17, 18, 20, 23, 26, 37, 41, 44, 45, 47, 54, 55, 56, 59, 61, 62, 63, 64, 65, 66, 67, 68, 71, 74, 77, 84, 85, 87, 89, 91, 92, 94, 100, 114, 128, 129, 138 and 156.

30. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 5, 6, 7, 16, 17, 18, 20, 23 and 26.

31. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 37, 41, 44, 45 and 47.

32. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 54, 55, 56 and 59.

33. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 61, 62, 63 and 64.

34. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 65, 66, 67, 68, 71, 74, 77 and 84.

35. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 85, 87, 89, 91, 92, 94, 100, 114, 128 and 129.

36. (New) The kit according to any one of claims 15, 16, 19 or 20 wherein at least one of the probes is selected from the group consisting of SEQ ID NO: 138 and 156.

37. (New) The kit of claims 19 or 20, further comprising a means for releasing, isolating, or concentrating polynucleic acids present in the sample.

38. (New) The kit of claims 19 or 20, further comprising at least one suitable set of primers.

39. (New) The kit according to claim 38, wherein the primer is selected from the group consisting of SEQ ID No: 162, 163, 164 and 39.

40. (New) The kit according to claim 38, wherein the set of primers is selected from the group consisting of

SEQ ID No: 162 and 163, and

SEQ ID No: 164 and 39.

41. (New) The kit of claims 19 or 20, wherein at least two probes are fixed to a solid support.

42. (New) The kit of claims 19 or 20, further comprising a means for detecting hybrids resulting from hybridization of at least one of the two probes to the sample.